REMARKS

Claim Objections

Claims 1, 8, 26, 31, 37 and 38 are objected to for the typographical error in which "Prosanosin" should be "Prosaposin". This error appears to be present only in claim 3, where it has now been corrected by amendement. Claims 8, 31 and 37 have been objected to for the term "expression of the cellular gene is detected by hybridization to a complementary nucleic acid". These claims have been amended as suggested by the Examiner. Claim 26 is objected to for an inadvertently inserted space. This error has not been detected. Claim 38 is objected to for grammatical errors. Claim 38 has been canceled.

Written Description

Claim 38 is rejected as not satisfying the written description requirement. Claim 38 has been canceled.

Anticipation

Claims 1, 2, 7, 26, 27, 30, 32, 33 and 36 are rejected as anticipated by Beug et al. (US 6,383,733). This rejection is further evidence by Yu et al., and Tremain et al. This rejection is overcome by amendment. Claims 1, 26 and 32 have been amended to specify that the senescence associated changes are induced by p21 and that the cells are tested in the presence of p21 expression.

To anticipate a claim, anticipation by a cited reference must be clear and unambiguous. It is not at all clear that the Beug reference anticipates the instant claims, because it is not at all clear that the culturing of the cells with TGFβ activates the PAI promoter through p21. It appears to be to the contrary. For example, Beug, at column 11, lines 34-50 reads as follows.

> This test cell, which is a human or animal cell, is stably transformed with a plasmid, in which a reporter gene, e.g. the luciferase gene, is under the control of the regulatory sequence of the PAI gene (or a gene which codes for another molecule regulated by TGFβ, e.g. for an extracellular matrix protein). The test cell is also transformed with the human type I or type II receptor, which was shown, after further tests, to be most efficient both at triggering the EF conversion and also at inducing PAI or another molecule regulated by TGFβ. The human TGFβ type II receptor used for the construction of the

> TβRII-dn is one of the possible target molecules for a TGFβ inhibitor. The control cell used is expediently a parallel clone in which the PAI-1 promoter controlled reporter gene is activated by another receptor not related to the TGFβ receptor.

Notably, for the Beug system to work, expression of the TGFβ receptor transgene is required. If another receptor is expressed in its place, it merely serves as a control. In the claimed invention, no construct encoding TGFβ is used or required. This strongly suggests that the system of Beug is acting quite differently than the claimed method.

This is further supported by the secondary references. Yu states that "We found that TNF-α but not TGF-β upregulates $p21^{waf1/cip1}$ expression". (emphasis added) Tremain adds, "Since $p21^{waf1}$ expression is elevated during senescence, and this does not appear to be mediated by TGFβ, it is likely that downstream signaling by p53 is intact." (emphasis added)

Taken together, culturing of the test cell with TGFβ, as taught by Beug, does not clearly and unambiguously utilize conditions that induce p21, and thus Beug does not anticipate the claimed invention.

Even if Beug is construed as activating p21, however, Beug looks for inhibitors of the TGFβ receptor. Thus the compounds of Beug would not be working in the presence of p21 expression, but rather would act by shutting off p21 expression.

Claims 1, 2, 6 and 8 are rejected as anticipated by Fisher and Jiang (US 6,051,376). In particular, col. 17, lines 45-50 of the reference are cited. Applicants note that in the cited passage, which is the only passage related to testing for compounds that inhibit senescence, Fisher does not include the claimed step of treating the cell with an agent that induces senescence or culturing the cell under conditions that induce senescence. While Fisher may later describe that a combination of IFNβ and MEZ irreversibly induces senescence, it does not include such treatment in its sole discussion of testing for inhibitory compounds. Rather, it appears to start with senescent cells and to test such cells for MDA7 expression (and its inhibition) in the presence of the compound. Moreover, while Fisher teaches that both MDA6 (p21) and MDA7 are expressed when a combination of IFNβ and MEZ is used to irreversibly induce senescence (Col. 109, l.53-56), it does not necessarily follow that MDA7 expression is being induced by p21. To the contrary, p21 reversibly induces senescence.

To anticipate a claim, a single reference must set forth every limitation of the claim. Accordingly, Fisher cannot anticipate claims 1, 2, 6, 8, 26, 27, 29, 31-33, 35 and 37. Applicants respectfully request that this rejection be withdrawn.

Obviousness

Claims 3, 28 and 34 are rejected as being obvious over Fisher and Jiang in view of Porter et al. As discussed above, Fisher is deficient in that it does not teach the step of treating the cell with an agent that induces senescence or culturing the cell under conditions that induce senescence in a method for identifying inhibitory compounds. Porter et al. does not remedy this deficiency. Accordingly, Applicants request that this rejection be withdrawn.

Obviousness-type double patenting

Claims 1-3 and 6-8 are rejected for obviousness-type double patenting over claims 1, 2, 4-8 and 1-14 of US Patent No. 6,706,491. Applicants will submit a terminal disclaimer to overcome this rejection once all other issues of patentability have been resolved.

Claims 1-3 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 28-37 and 58-63 of co-pending application no. 10/233,032. This rejection is provisional because neither the presently pending claims nor the claims of the co-pending application have been allowed. Under PTO practice, this rejection will be withdrawn when all other issues of patentability have been favorably resolved. Accordingly, Applicants will not address this rejection at this time.

Claims 1-3 and 6-8 are provisionally rejected for obviousness-type double patenting over claims 25-30, 32, 33, 52-58, 95-101, 103-105 and 107-115 of co-pending application no. 09/861,925. This rejection is provisional because neither the presently pending claims nor the claims of the co-pending application have been allowed. Under PTO practice, this rejection will be withdrawn when all other issues of patentability have been favorably resolved. Accordingly, Applicants will not address this rejection at this time.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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